EVIDENCE SUMMARY

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From the Society for Vascular Surgery

Best management options for chronic iliac vein stenosis and occlusion

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Background: **Iliac vein stenting technology is rapidly emerging as a minimally invasive alternative to traditional open venovenous bypass procedures for iliac vein stenoses and chronic total occlusions.**
Methods: **Peer-reviewed publications meeting eligibility criteria were retrieved and reviewed from public domain databases.**
Results: **Reviewed reports encompass ~1500 patients. Evidence quality was judged moderate, with a grade 1B recommendation (benefits outweigh risks) for patients with disabling symptoms in whom conservative therapy had failed. A grade 2B recommendation was assigned for patients with less severe symptoms. Iliac vein stenting is safe, with negligible morbidity (<1%). Patency was 90% to 100% for nonthrombotic disease and 74% to 89% for post-thrombotic disease at 3 to 5 years. Clinical relief of pain was 86% to 94%, and relief from swelling was 66% to 89%. From 58% to 89% of venous ulcers healed. Procedural success in recanalization of chronic total occlusions was 83% to 95%. Hybrid techniques for complex cases are in evolution.**
Conclusions: **Iliac vein stenting is emerging as a safe and effective alternative to traditional open surgery to correct iliac vein obstruction. (J Vasc Surg 2013;57:1163-9.)**

Venous stent technology has rapidly evolved as the initial procedure of choice in the treatment of iliofemoral stenosis and chronic total occlusions (CTO). Open surgery, the prior standard, is now reserved only for stent failures. Concurrently, the use of intravascular ultrasound (IVUS) imaging, essential for proper stent placement, has broadened the scope of stent treatment to include primary nonthrombotic iliac vein lesions (NIVL). Previously, obstruction in this genre was thought to be relatively rare, largely due to the poor diagnostic sensitivity of venography.

The pivotal role of iliac vein stenoses as a cause of recurrent thrombosis and in the development of post-thrombotic syndrome (PTS) is now well recognized. Clinical relief, including ulcer healing, occurs with iliac vein stenting even in the presence of significant reflux, an intriguing finding with fundamental pathophysiologic implications.

Iliac vein stenting appears to be safe and effective, as reviewed below; the technique is easier to learn and use than open surgery, potentially benefitting a larger proportion of patients. Because open surgery is not precluded afterwards, iliac vein stenting is in a different class from traditional venous bypass techniques, and strict efficacy comparisons are moot in a disease that seldom poses a threat to limb or life. Accordingly, this evidence review focuses on the iliac vein stent literature, and some key references to open procedures are included to provide context.

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METHODS

Peer reviewed articles in English were retrieved from public domain databases with the following search terms: "common iliac vein; iliac vein; iliofemoral vein; stenosis; venous occlusion; postthrombotic syndrome; May-Thurner syndrome; Cockett syndrome; iliac vaso compression syndrome," and "venous stent." All were listed in Medline. The voluminous literature dealing with acute occlusions was excluded because disease progression is likely different. For outcome analysis, a selection threshold of at least 25 limbs treated for chronic occlusions with a minimum follow-up of 3 years was applied. None that met the threshold were excluded; some below the threshold and ancillary references have been selectively included to highlight special features of interest.

RESULTS

All studies reviewed are single-arm retrospective case series. The quality of evidence[1] for stent treatment was graded as moderate. The consistency of the evidence and the magnitude of effects, such as ulcer healing, for example, suggest a grade 1B recommendation (strong recommendation, benefits outweigh risks) for patients with disabling symptoms in whom conservative therapy has failed. Complex surgical procedures, such as venovenous bypass

Table I. Incidence and diagnosis of iliac vein obstruction

First author, year	*Comments*
Negus,[5] 1967	Exercise femoral pressure parameters to diagnose iliac vein obstruction
Negus,[6] 1968	Poor sensitivity of venography; incidence in general population
Thomas,[7] 1967	Technique of iliac venography; description of collaterals
Raju,[8] 2011	Poor sensitivity of venography; diagnostic accuracy with combination of techniques
Hurst,[9] 2001	Use of IVUS for the diagnosis of iliac vein obstruction
Neglen,[10] 2002	Superiority of IVUS imaging over venography for diagnosis
Forauer,[11] 2002	IVUS guidance essential for proper stent placement
Raju,[4] 2006	IVUS imaging features of thrombotic and nonthrombotic lesions. High prevalence of the lesion in nonthrombotic disease
Marston,[12] 2011	Sensitivity of MR and CT imaging to detect iliac vein obstruction
Kibbe,[13] 2004	Frequent prevalence of the lesion (CT) in silent form in the general population

CT, computed tomography; *IVUS,* intravascular ultrasound; *MR,* magnetic resonance.

Table II. Techniques of correcting iliac vein obstruction

First author, year	*Comments*
Halliday,[17] 1985	Palma bypass; 47 PTS limbs. Venographic cumulative patency of 75% at 5 years
Jost,[18] 2001	18 Palma bypass • 17 prosthetic bypass • 6 spiral vein bypass • 1 vein patch • 62% overall cumulative patency at 3 years and 83% for Palma bypass at 4 years
Puggioni,[19] 2004	Technique of endophlebectomy
Garg,[20] 2011	Hybrid and open techniques of correction
Neglen,[21-25] 2000-2010	Technique of iliac vein stenting; need for large stents and extension into inferior vena cava. Stent extension across inguinal ligament. Bilateral iliac vein stents. Stenting across stenotic/occluded IVC filters. Incidence of ISR after iliac vein stent
Raju,[26] 2009	CTO recanalization technique
Kolbel,[27] 2009	Jugular approach for CTO recanalization; ancillary techniques
Raju,[28] 2009	Different types of stent malfunction and reinterventional techniques to correct them

CTO, Chronic total occlusions; *ISR,* in-stent restenosis; *IVC,* inferior vena cava; *PTS,* post-thrombotic stenosis.

or deep valve reconstruction, were the only available options for such patients before. A grade 2B recommendation was assigned for patients with less severe symptoms.

Clinical features and pathophysiology

Symptomatic iliac-caval obstruction of NIVL or PTS etiology can present with a wide range of clinical features, including all clinical CEAP classes. Specific correction is seldom warranted unless advanced symptoms (CEAP clinical class ≥3 or significant pain). Orthostatic limb pain is a pervasive feature but may be absent in ~20% to 30% of patients; it may be the only clinical manifestation sans other clinical features in 10% to 15% of patients (CEAP ≤2). Excellent pain relief may be obtained by stent treatment.[2] Recurrent cellulitis, especially the spontaneous variety, may be indicative of an underlying iliac obstructive lesion amenable to correction and relief.[3] Iliac vein thrombosis secondary to an obstructive lesion is well known, with a voluminous literature that is not reviewed here.

A confusing feature is the presence of iliac caval pathology in a wide swath of the general population in silent form. This has been a source of controversy in attributing pathologic significance to a ubiquitous lesion. A possible explanation to connect progression of a silent lesion into a symptomatic one is the concept that the lesion functions in a permissive fashion.[4] Regardless, there is little doubt that correction of iliac stenosis remits symptoms if they occur.

Diagnosis

Diagnosis of iliac-caval obstruction remains hobbled by the relative insensitivity of contrast venography (Table I). This is because many iliac vein lesions are visible only in one plane and membranous lesions may not be visible at all. Perivenous and wall fibrosis are impervious to venography; diffuse long stenoses common in post-thrombotic disease are easily missed. Computed tomography or magnetic resonance imaging techniques may have similar sensitivity issues,[12] but comparative studies to assess diagnostic accuracy are as yet unavailable.

Intravascular ultrasound (IVUS) imaging has emerged as a promising new diagnostic tool with apparently higher sensitivity and greater diagnostic yield (Table I). Previously, symptomatic NIVL incidence was thought to be relatively rare, with ~3% of the population with chronic venous disease involving predominantly the left lower limb of young women. Use of IVUS imaging has shown that iliac-caval obstructions occur as commonly in nonthrombotic cases as in post-thrombotic limbs, affecting both sexes, all age groups, and both sides.

This lesion, first described by McMurrich in 1908, was more clearly defined by several authors, notably by May and Thurner (1957) and later Cockett (1965-1967). Earlier autopsy studies[14] and current IVUS findings clearly indicate that NIVL are complex lesions involving not only external compression but also wall fibrosis, intraluminal webs, and membranes. The term "iliac compression syndrome" is, therefore, a misnomer.

The lesion is clearly nonthrombotic because it lacks the pathognomic vascular invasion. A traumatic etiology from pulsations of the intimately related artery is probably the major cause, although an ontogenic origin is likely in some, because the lesions, particularly membranous ones, occur at embryologic fusion planes.[14,15] The lesion has

Table III. Technical outcome of iliac vein stenting

First author	*Limbs, No. (%)*	*Case mix NIVL/PTS, No. (%)*	*Cumulative patency*			*Duration cumulative f/u, years*	*Complications (No. of limbs)*	*Remarks*
			Primary	*Primary assisted*	*Assisted*			
Open and hybrid (with stent) reconstruction								
Garg,[20] 2011	68 52 open 12 hybrid	NIVL, 5/68 (7) PTS: 63/68 (93)	42%	47%	59%	5	Superficial wound infection (2) Lymphocele (3) Wound hematoma (2) No death No PE	Stenting below inguinal ligament increased stent patency in hybrid reconstructions
Stent								
Gutzeit,[29] 2011	15	Iatrogenic: 6/15 (40) PTS, 9/15 (60)	100%	100%	100%	22 14 mean	Stent fracture (1) with patency	Up to 22-year f/u with no occlusions in 15/20 with f/up
Hartung,[30] 2009	89 30/89 (34) CTO	NIVL: 52/89 (58) PTS: 35/89 (39) Congenital: 2/89 (3)	83%	89%	93%	7	2 stent migrations 2 access site hematomas 1 femoral artery tear 2 contrast extravasation in CTO Unrelated death (1) DVT (5)	93% technical success in CTO No PE CFV involvement and post-thrombotic disease decreased patency Reintervention in 8% Thrombophilia in 20% did not affect patency
Knipp,[31] 2007	58	PTS: 52/58 (90)	38%	63%	74%	5	1 retained balloon	58 stent procedures, 17% with recent thrombus; recent trauma, male sex and age <40 years decreased patency which decreased from 63% at 5 years to 29% and 0% for ≥2 risk factors, respectively
		NIVL: 6/58 (10)					1 stent migration 1 groin hematoma 1 retroperitoneal hematoma	Thrombophilia in 19 did not affect patency
Meng,[32] 2011	272	NIVL: 272/272 (100)	94%	NA	NA	5		Type of stent used not mentioned
Neglen,[2] 2007	982	NIVL: 518/982 (53)	NIVL: 79%	100%	100%	6	4 femoral artery injury	Thrombophilia in 38% did not affect patency
		PTS: 464/982 (47)	PTS: 57%	80%	86%		1 guidewire trapped in stent 1.5% DVT/stent thrombosis <30 days post-op 3% DVT/stent thrombosis >30 days post-op No mortality No pulmonary embolus	Ambulatory venous pressure and hand/foot pressure improved ISR (>50%) occurred in 10% in PTS and 1% in NIVL at 6 years

Table III. Continued.

First author	*Limbs, No. (%)*	*Case mix NIVL/PTS, No. (%)*	*Cumulative patency*			*Duration cumulative f/u, years*	*Complications (No. of limbs)*	*Remarks*
			Primary	*Primary assisted*	*Assisted*			
Ye,[33] 2012	224	NIVL: 100%	99%	99%	99%	4	Local stent migration (3) Back pain (34) No mortality No DVT or PE	
Recanalization of CTO								
Kolbel,[27] 2009	59	PTS: 66%	67%	75%	79%	5	1 access-site bleed	Technical success 95%
		Other: 34%					2 perforations requiring transfusion	Stented below inguinal. Ligament in 70% did not affect outcome
							No PE	Thrombophilia in 67% did not affect patency
Raju,[26] 2009	139	PTS: 100%	32%	58%	66%	4	Back pain: 25% 1 transient rise in contrast-related creatinine DVT/stent thrombosis <30 days: 10/139 (7) DVT/stent thrombosis >30 days: 32/139 (23) No bleeding complications including in stents across IVC filters	83% technical success 14 across IVC filters did not affect patency Thrombophilia in 34% did not affect patency
Rosales,[34] 2010	34	PTS: 100%	67%	76%	90%	7	DVT: 11/34 (32)	94% technical success 65% stented below inguinal ligament Thrombophilia did not affect patency

CTO, Chronic total occlusion; *DVT*, deep venous thrombosis; *f/u*, follow-up; *ISR*, in-stent restenosis; *IVC*, inferior vena cava; *NA*, not available; *NIVL*, nonthrombotic iliac vein lesions; *PE*, pulmonary embolus; *PTS*, post-thrombotic syndrome.

been occasionally discovered in young children.[14,16] Intraperitoneal fibrosis, tumor, and other extrinsic causes of iliac vein obstruction are relatively rare, accounting for ~5% of cases.

Treatment options

A variety of open, closed, and hybrid techniques are now available for treating iliac vein obstructions (Table II).

Evidence summary

Technical outcome of iliac vein stenting. Stent treatment appears to be a safe procedure. Among the ~1500 patients in the series reviewed, no deaths or pulmonary embolus were reported. Access site complications occurred in <1% and significant bleeding requiring transfusions in <0.03%. The incidence of postoperative and interval long-term deep venous thrombosis appears to be no different from the incidence of native disease. Stent-related complications, such as stent fracture, erosions, late embolization, and infections, are extremely rare. It is not clear if this is related to the specific type of stent used. All of the reviewed series, except one (information missing), reported using self-expanding large-caliber Wallstents (Boston Scientific, Natick, Mass) in most of the patients. Other complications, such as back pain, occur early after the procedure and are generally minor and self-limited.

Stent patency (Table III) has been surprisingly good, considering the propensity for thrombosis in the venous system with low velocity flow. Stent thrombosis is an extreme rarity in NIVL disease as reported, an astonishing statistic considering arterial stent experience. Approximately 25% of stents occlude in thrombotic cases during a 3- to 5-year period. Secondary patency has ranged from 90% to 100% in NIVL limbs and from 74% to 89% in post-thrombotic limbs during 4 to 7 years. Patency is somewhat lower, at 66% to 89% at 4 to 7 years, and stent occlusions higher in the group among CTO recanalizations. Factors associated with stent occlusion include prior thrombosis, male sex, recent trauma, and age <40 years, with a combination of factors exponentially decreasing

Table IV. Clinical outcome of corrective procedures for iliac vein obstruction

First author, year	*Limbs*	*CEAP*	*Ancillary procedures*	*Clinical outcome*	*Follow-up, months*	*Comments*
Open surgical correction (venovenous bypass)						
Jost,[18] 2001	42	C_0: 10% C_2: 2% C_3: 45% C_4: 10% C_5: 12% C_6: 21%		Moderate Improvement in outcome score with patent grafts. 7/9 ulcers healed	72	…
Open and hybrid (with stent) reconstruction						
Garg,[20] 2011	64	$C_{0\text{-}2}$: 2 C_3: 30 C_4: 12 C_5: 8 C_6: 12		60% no pain & no or minimal swelling 50% ulcer healing	Median: 41	
Stent correction						
Gutzeit,[29] 2011	15			Thigh size normalized	Mean: 168	
Hartung,[30] 2009	89	C_2: 15 C_3: 59 C_4: 7 C_5: 2 C_6: 6	3 ovarian vein embolization 5 superficial vein procedures	43/45 improvement in pain; in 31 complete relief 5/6 (83%) ulcers healed 23/26 pelvic congestion improved; 15 cured	Median: 38	
Knipp,[31] 2007	63	C_3: 47 C_4: 12 C_5/C_6: 4	28 thrombolysis 6 AV fistula 18 IVC filters	Significant clinical improvement in 80%; no change in 20%	Mean: 30	Mix of acute and chronic cases
Meng,[32] 2011	296 272/296 stented	C_2: 55 C_3: 238 C_4: 133 C_5: 11 C_6: 78	170 saphenous vein high ligation and stripping 24/296 POBA only	Resolution of swelling: 84% 87% with skin pigmentation showed improvement 85% ulcers healed	Median: 46	
Neglen,[2] 2007	982	C_2: 7% C_3: 47% C_4: 24% C_5: 5% C_6: 17%	197 GSV/SSV ablations	Severe leg pain (VAS >5) decreased from 54% to 11%; cumulative total relief of pain in 62% Severe swelling (grade 3) decreased from 44% to 18%; cumulative total relief of swelling in 32% 58% (cumulative) of ulcers healed Significant QOL improvement in all categories	Cumulative: 60	Symptom relief reported on cumulative basis
Ye,[33] 2012	224	C_0: 5% C_1: 1% C_2: 3% C_3: 37% C_4: 12% C_5: 15% C_6: 28%	132/224 (59%) EVLA	Edema relief: 89% Ulcer healing: 82% Pain decreased from 4.3 to 0.4 (VAS) QOL significantly improved	Mean: 50	

Table IV. Continued.

First author, year	*Limbs*	*CEAP*	*Ancillary procedures*	*Clinical outcome*	*Follow-up, months*	*Comments*
Recanalization of CTO						
Kolbel,[27] 2009	66	C_3: 22 C_4: 17 C_5: 12 C_6: 8		23% asymptomatic 52% improved 20% same 6% worse	Median: 32	Thrombophilia did not affect outcome
Raju,[26] 2009	139	C_2: 3		Cumulative improvement in pain: 79%; complete relief in 67%	Median: 48	
		C_3: 71		Cumulative improvement in swelling: 66%		
		C_4a: 14		Cumulative healing of ulcers: 56%; complete relief in 32%		
		C_4b: 8		58% of ulcers healed		
		C_5: 11		QOL significantly improved		
		C_6: 32				
Rosales,[34] 2010	34	C_3: 27		Swelling and pain was resolved in 32/34 (94)	Median: 33	Thrombophilia did not affect outcome
		C_6: 7		4/7 (57) ulcers healed		

AV, Arteriovenous; *GSV,* great saphenous vein; *IVC,* inferior vena cava; *QOL,* quality of life; *SSV,* small saphenous vein; *VAS,* visual analog scale.

long-term patency.[31] Thrombophilia did not affect stent outcome in several series. Technical success of CTO recanalizations has ranged from 83% to 95%.

Mild in-stent restenosis (ISR) is common, but significant lesions (≥50%) occur in ~10% of post-thrombotic cases; it is extremely rare in the NIVL subset (1%). ISR incidence is related to thrombophilia, prior thrombosis, and use of a long stent.[21] Limited experience indicates that pregnancy can be tolerated after placement of self-expanding stents.[35]

Use of anticoagulation during and after stent placement has varied. Although some authors have used postoperative warfarin anticoagulation for several months after the procedure, it does not seem to be necessary in NIVL.[2,30,31] Patency rates appear not to be affected with use of only aspirin after stent placement in this subset.

Clinical outcome. Clinical relief has been good to excellent, as reported, and the results appear to be durable (Table IV). Relief of pain is excellent, ranging from 86% to 94%, with total relief in most. Swelling relief is good, ranging from 66% to 89%. Interestingly, ulcer healing occurs in 58% to 89% of patients after stent placement, even without correction of associated reflux.[36,37] Two of the larger series reported improvement in quality of life parameters.

Iliac vein stents have been placed in stenosed or occluded iliac veins to maintain dialysis access and in pediatric patients with congenital heart defects to gain access for catheterization.[38] Iliac vein occlusion may lead to neurogenic claudication due to collateral congestion in the spinal canal affecting the cord or cauda equina; diagnosis is made with magnetic resonance or computed tomography imaging. Relief with iliac vein stenting has been reported.[39] One reviewed series[30] reported relief of pelvic congestion in a large subset after iliac vein stent placement.

Areas needing further study. Many areas related to iliac vein stenting require further study and clarification, including the role of IVUS imaging (used in only two studies), the degree of correctible stenosis, the relationship between silent and symptomatic obstructions, interrelationship of obstruction and reflux, and finally, a hemodynamic metric for obstruction.

CONCLUSIONS

Stent placement to correct iliac-caval-femoral obstructions is emerging as a safe, effective, and minimally invasive alternative to traditional open surgery.

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